REMARKS/ARGUMENTS

Upon entry of this Amendment, claims 1, 6-12 and 15-18, are pending and are presented for examination. Claims 2-5 have been withdrawn as being directed to a non-elected invention pursuant to a Restriction Requirement. In order to expedite prosecution, claims 1, 6-11 and 18, have been amended and claims 13 and 14 have been cancelled without prejudice to further prosecution. No new matter has been added by the amendments to the claims. Accordingly, reconsideration is respectfully requested.

I. Rejections under 35 U.S.C. §112

A. Indefinite Rejection

Claim 18 was rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regard as his invention.

In order to expedite prosecution, Applicants have amended claim 18 to incorporate the definitions of four substituents R^1, R^2, R^3 and Q. In view of the amendment to claim 18, the Examiner's concern is overcome. Accordingly, Applicants urge the Examiner to withdraw this rejection under 35 U.S.C. §112, second paragraph.

B. Written Description Rejection

Claims 1, 6-12 and 15-19 were rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the Written Description requirement. The Examiner asserts that the instant claims contain subject matter that was not described in the specification.

In order to expedite prosecution, Applicants have amended claims 1, 6-11 and 18. Support for the amendments to each claim is provided below:

Support for the amendments to claim 1 is found in the originally filed claim 1; and on page 2, *i.e.*,, paragraphs 7, 9 and 11. For example, paragraph 7 and originally filed claim 1 recite X^1 and X^2 are independently selected from the group consisting of -N= and $-CR^4$.

Support for the amendments to claim 6 is found, for example, in the definition of R^7 in the originally filed claim 6 and on pages 7-8, *i.e.,* paragraph 41.

Support for the amendments to claim 7 is found, for example, in the originally filed claim 7 and on page 9, *i.e.,* paragraph 45.

Support for the amendments to claim 8 is found, for example, in the originally filed claim 8 and on pages 9-10, *i.e.,* paragraph 46.

Support for the amendments to claim 9 is found, for example, in the originally filed claim 9 and on page 10, *i.e.,* paragraph 47.

Support for the amendments to claim 10 is found, for example, in the originally filed claim 10 and on page 10, *i.e.,* paragraph 48.

Support for the amendments to claim 11 is found, for example, on page 5, *i.e.,* paragraph 29; and on page 17, *i.e.,* paragraph 69.

Support for the amendments to claim 18 is found, for example, on pages 21-22, paragraphs 96-99; on pages 26-27, Example 9; on page 42, compounds 114-119; and on page 43, compounds 120-121 and 123.

In view of the amendments to the claims and the support for the claim amendments provided above, it is clear that claims 1, 6-12 and 15-19 are fully supported by the specification as originally filed. Accordingly, Applicants urge the Examiner to withdraw this rejection under 35 U.S.C. §112, first paragraph.

C. Enablement Rejection

1. Solvate or Hydrate

Claims 1, 6-12 and 15-19 were rejected as allegedly non-enabled by the specification for making solvates or hydrates of the claimed compounds. In support of this rejection, the Examiner alleges that the formation of solvates or hydrates and composition of solvates or hydrates are unpredictable. Therefore, in the absence of working examples, the

Examiner alleges that undue experimentation would be required to make Applicants' invention. Applicants respectfully disagree.

The test for the enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue (*see*, MPEP §2164.01). The court has stated eight unlimited factors to assess whether experimentation is undue. Applicants assert that, if anything, only routine experimentation is needed to form solvates or hydrates of the presently claimed compounds.

The nature of the invention and the state of prior art. The Examiner alleges that the state of art is such that it is not predictable whether solvates or hydrates of a compound will form or what the composition will be (*see*, page 5 of the Office Action, citing page 358 of Anthony R. West, *Solid State Chemistry and Its Applications*, Wiley, hereinafter "West"). In traversal of the rejection, Applicants submit that West is ***not*** analogous art.

To rely on a reference as a basis for rejection of an applicant's invention, the reference must either be in the field of applicant's endeavor or if not, then be reasonably pertinent to the particular problem with which the inventor was concerned (*see*, MPEP §2141.01(a)). A perusal of the West reference reveals that West is directed to inorganic salts and the hydrates or solvates of such inorganic salts. West teaches the formation of hydrates or solvates of inorganic salts at salt-melting temperatures, typically in the range of several hundred to greater than one thousand degrees Celsius. In contrast to West, the present invention is directed to hydrates of organic pyrimidine, pyridine or triazine derivatives formed at low temperatures. Hence, West is in a field that is quite different from that of the present invention.

Furthermore, the principles surrounding the formation of solvates or hydrates of inorganic salts are very different from that the principles surrounding the formation of solvates or hydrates of organic compounds, such as pyrimidines, pyridine or triazine derivatives. Inorganic salts in West form hydrates through ionic interaction at high salt-melting temperatures, whereas the hydrates of the organic compounds of the present invention are formed through van der Waals or hydrogen bonding interactions. Moreover, the high salt-melting conditions taught by West would result in the decomposition of organic compounds if such conditions were to be used

in the formation of the organic hydrates of the present invention. Therefore, West is not reasonably pertinent to the particular problem with which Applicants were concerned. As such, West is not an analogous reference.

As stated above, the test for enablement is not whether any experimentation is necessary. The court states that the test is not merely quantitative, since a considerable amount of experimentation is permissive, if it is merely ***routine***, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed (*see*, MPEP §2164.06).

Here, recrystallization is a routine method and well-known to a person of skill in the art for the isolation and purification of organic compounds. It is also a common observation, which is well-known to persons skilled in the art, that organic compounds form solvates or hydrates during the recrystallization and purification processes. For example, hydrates or solvates of the claimed compounds can be conveniently formed by recrystallization (*see*, page 15, paragraph 64 of the specification). Therefore, if anything, the formation of hydrates or solvates only requires a minimal amount of routine experimentation, which is permissible and not undue.

In concluding that the formation of hydrates is unpredictable, the Examiner refers to an article by Vippagunta *et al.* (*Advanced Drug Delivery Reviews*, 2001, 48, 3-26, hereinafter "Vippagunta"), stating that predicting the formation of hydrate may be difficult. However, the article also points out that a large number of pharmaceutically active compounds, approximately one-third, are ***predictably*** capable of forming hydrates (*see*, Vippagunta, page 15). ***In fact, the interaction of drugs with water often results in the formation of hydrates*** (*see*, Stahl, "The problems of drug interactions with excipients," in D.D. Braimar, *Towards Better Safety of Drugs and Pharmaceutical Products*, Elsevier/North-Holland Biomedical Press, 1980, page 271, a copy of which was attached as Exhibit A provided in the previous response). If one skilled in the art can readily anticipate the effect of a change within the subject matter to which the claimed invention pertains, then there is predictability in the art (MPEP §2164.03). The compounds of the present invention have extended planar aromatic or heteroaromatic rings. It is well known in

the art that such compounds have a tendency to crystallize. In particular, it is well known to a person skilled in the art that the nitrogen atom(s) in the aromatic rings can readily form hydrogen bonds with water, which facilitates the formation of hydrates (*see*, U.S. Patent No. 4,839,112, columns 2 and 3). Hydrogen bonding also plays an important role in the formation of hydrates of organic compounds (Lowry *et. al.*, Mechanism and Theory in Organic Chemistry, 4th Ed; page 283). Hence, based on the structure of the compounds, one skilled in the art can readily predict whether the compounds of the present invention will form hydrates. Thus, if anything, only reasonable and routine experimentation is needed to find out whether the compounds can form hydrates (*see*, page 15, paragraph 64 of the specification).

Working examples/amount of guidance. The Examiner also alleges that there are no working examples of a solvate or a hydrate. As set forth in MPEP §2164.02, the specification need not contain an example if the invention is otherwise disclosed in such a manner that one skilled in the art will be able to practice it without undue experimentation. Here, as discussed above, those of skill in the art know that the compounds of the present invention have a tendency to crystallize and, if anything, only routine experimentation is needed to isolate the hydrates and confirm their compositions. Hence, undue experimentation is not required even in the absence of working examples.

Breadth of claim and quantity of experiment. The Examiner alleges that the amount of experimentation would be undue because the genus embraces a large number of compounds. Again, Applicants respectfully disagree that the experimentation will be undue. Although there are a number of compounds embraced by the formulae in the claimed invention, all of the compounds have similar planar hetero-aromatic ring structures containing one, two or three nitrogen atoms, which can readily form hydrogen bonds with water. A person skilled in the art will also recognize that minor variations of the substituents is unlikely to have significant effects on the formation of hydrates. Therefore, if anything, a person of skill in the art only needs to conduct routine experimentation to determine whether the compounds form hydrates and to confirm their compositions.

In view of the fact that undue experimentation is not required for the formation of solvates or hydrates of the claimed compounds, the solvates or hydrates of the claimed compounds do, in fact, meet the enablement requirement. Accordingly, Applicants respectfully request that the enablement rejection of the solvates or hydrates under 35 U.S.C. §112, first paragraph, be withdrawn.

2. Claims 15-16

Claims 12-16 were rejected under 35 U.S.C. §112, first paragraph, as allegedly being non-enabled for treating tumoral diseases as recited in the claims. The Examiner takes the position that claim 12 encompasses thousands of cancers and the claimed method of treating is solely based on the inhibitory activity disclosed for the compounds. Applicants respectfully traverse the rejection.

Applicants submit that claims 15-16 are fully enabled by the specification as filed. As set forth in the Example Section of the present application (*see, e.g.*, pages 44-45) as well as the reference by Adrian *et al.* (provided to the Examiner as Exhibit C in the previous response), the compounds of the present invention are a new class of Bcr-abl inhibitors that have the ability to selectively inhibit the proliferation of Bcr-abl-transformed cells and have anti-proliferative activity on Ba/F3 cells expressing either wild type or mutant forms of Bcr-abl. The examples also demonstrate that the compounds of the present invention, which inhibit the proliferation of the Bcr-abl expressing cells, inhibit cellular Bcr-abl autophosphorylation in a dose-dependent manner. Therefore, claims 15-16 are fully enabled by the specification as originally filed. Accordingly, Applicants respectfully request that the enablement rejection of claims 15-16 under 35 U.S.C. §112, first paragraph, be withdrawn.

II. Rejections under 35 U.S.C. § 102(b)

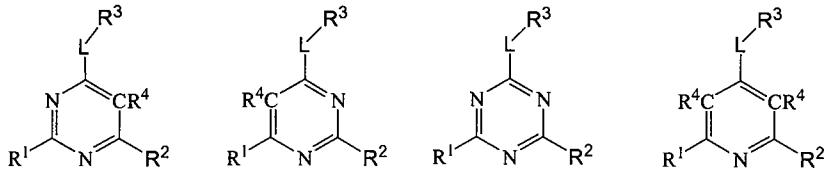
A. Rejection of Claims 1, 6-8 and 11 Over Boykin *et al.*

Claims 1, 6-8 and 11 were rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Boykin *et al.* (U.S. Patent No. 5,686,456, hereinafter "Boykin"). To expedite

prosecution, Applicants have amended claims 1, 7, 8, 9 and 10. In view of the amendments, Applicants respectfully traverse the rejection.

As set forth in MPEP §2131, a claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference.

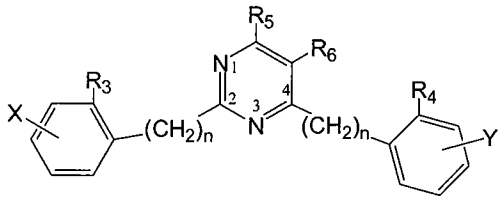
With X^1 and X^2 being nitrogen and/or a substituted carbon, the compounds of Formula I have four possible core structures, *i.e.*,, $\mathbf{I^A}$, $\mathbf{I^B}$, $\mathbf{I^C}$ and $\mathbf{I^D}$, as illustrated below:



$\mathbf{I^A}$ $\mathbf{I^B}$ $\mathbf{I^C}$ $\mathbf{I^D}$

The substituents R^1, R^2, R^3, R^4 and L are defined as in amended claim 1. In view of the Restriction Requirement, the remarks below will only address structures $\mathbf{I^A}$ and $\mathbf{I^B}$ of Formula I, which are the only structures under examination.

Applicants assert that Boykin does not teach each and every element of the claimed invention. Boykin discloses pyrimidine derivatives having the structure:



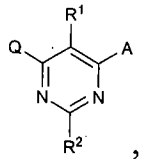
wherein n is a number from 0 to 2. The substituents at the 2 position of the above Boykin structure are either aryl (n = 0) or arylalkyl (n = 1 or 2) groups. The substituents at the 2 position of the above Boykin structure corresponds to either R^1 in structure $\mathbf{I^A}$ or R^2 in structure $\mathbf{I^B}$. Applicants submit that Boykin does not disclose compounds having structures $\mathbf{I^A}$ or $\mathbf{I^B}$ as recited in amended claim 1. As recited in claim 1, R^1 in structure $\mathbf{I^A}$ is $-X^3NR^6R^7$ (amino, X^3 = bond; or aminoalkyl, X^3 = alkylene) or $-X^3OR^7$ (alkoxy or aryloxy, when X^3 = bond; or alkoxyalkyl or aryloxyalkyl, when X^3 = alkylene); R^2 in structure $\mathbf{I^B}$ is hydrogen, halo, amino, $C_{1\text{-}4}$alkyl, halo-

substituted C_{1-4}alkyl, C_{1-4}alkoxy or halo-substituted C_{1-4}alkoxy. Neither R^1 in structure $\mathbf{I^A}$ nor R^2 in structure $\mathbf{I^B}$ recite an aryl or an arylalkyl substituents as disclosed in Boykin. Hence, Boykin does not teach the compounds of Formula I recited in claim 1 and, thus, claim 1 is not anticipated by Boykin. Since claims 6-8 and 11 are dependent from claim 1 and therefore incorporate all the limitations of claim 1, claims 6-8 and 11 are not anticipated by Boykin. Accordingly, Applicants respectfully request that the rejection of claims 1, 6-8 and 11 over Boykin under 35 U.S.C. §102(b) be withdrawn.

B. Rejection of claims 1, 6-8 and 11 over Carling *et al.*

Claims 1, 6-8 and 11 were rejected under 35 U.S.C. 102(b) as allegedly being anticipated by Carling *et al.* (U.S. Patent No. 5,763,448, hereinafter "Carling"). Applicants respectfully traverse the rejection.

Applicants assert that none of the core structures $\mathbf{I^A}$ or $\mathbf{I^B}$ of Formula I are anticipated by Carling because Carling does not teach each and every element of the claimed invention. Carling discloses a compound, *i.e.*,, a pyrimidine derivative, having the formula:



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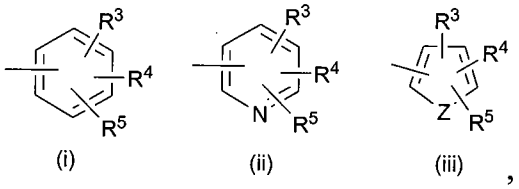
wherein Q represents a substituted five- or six-membered monocyclic hetero-aliphatic ring, which contains one nitrogen atom as the sole heteroatom and is linked to the pyrimidine ring via a carbon atom; and A represents a group of formula (i), (ii) or (iii):



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wherein Z represents oxygen, sulfur or NH. The substituent Q is a heterocycloalkyl. The substituent A is a heteroaryl. Carling discloses compounds having a combination of heterocycloalkyl and heteroaryl substituents at the respective Q and A positions.

Applicants assert that Carling does not teach structure $\mathbf{I^A}$. Substituents Q and A on the pyrimidine ring in Carling occupy the positions that correspond to substituents L-R^3 and R^2 in structure $\mathbf{I^A}$. As set forth above, Carling discloses Q being heterocycloalkyl and A being heteroaryl. Carling does not disclose Q or A being hydrogen, halo, amino, C_{1-4}alkyl, halo-substituted C_{1-4}alkyl, C_{1-4}alkoxy or halo-substituted C_{1-4}alkoxy as recited for R^2 in structure $\mathbf{I^A}$. As such, Carling does not teach structure $\mathbf{I^A}$ of Formula I of amended claim 1 and, thus, structure $\mathbf{I^A}$ is not anticipated by Carling.

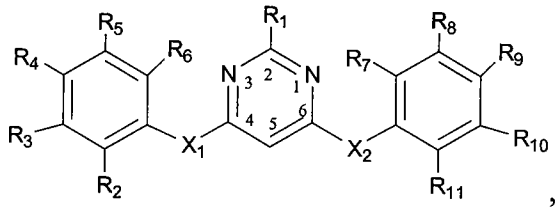
Applicants further assert that Carling does not teach structure $\mathbf{I^B}$. Substituents Q and A on the pyrimidine ring in Carling occupy the positions that correspond to substituents L-R^3 and R^1 in structure $\mathbf{I^B}$. As set forth above, Carling discloses Q being heterocycloalkyl and A being heteroaryl. Carling does not disclose or suggest Q or A being $-X^3NR^6R^7$ (amino, when X^3 = bond; or aminoalkyl, when X^3 = alkylene) or $-X^3OR^7$ (alkoxy, aryloxy or heteroaryloxy, when X^3 = bond; or alkoxyalkyl, aryloxyalkyl or heteroaryloxyalkyl, when X^3 = alkylene) or $-X^3$-aryl (aryl, when X^3 = bond; or arylalkyl, when X^3 = alkylene). Hence, Carling does not teach structure $\mathbf{I^B}$ of amended claim 1, and, thus, structure $\mathbf{I^B}$ is not anticipated by Carling.

Accordingly, Applicants respectfully request that the rejection of claim 1 under 35 U.S.C. §102(b) over Carling be withdrawn. Moreover, since claims 6-8 and 11 are dependent from claim 1 and, therefore, incorporate all the limitations of claim 1, claims 6-8 and 11 are not anticipated by Carling. Accordingly, Applicants respectfully request that the rejection of claims 1, 6-8 and 11 over Carling under 35 U.S.C. §102(b) be withdrawn.

C. Rejection of claims 1, 6, 9, 10 and 17 over Cuccia *et al.*

Claims 1, 6, 9, 10 and 17 were rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Cuccia *et al.* (U.S. Patent No. 6,281,219, hereinafter "Cuccia"). To the extent that the rejection is applicable to amended claim 1, Applicants respectfully traverse the rejection.

Applicants assert that Cuccia does not teach each and every element of the claimed invention and, thus, Cuccia does not anticipate the claimed invention. Cuccia teaches pyrimidine derivatives having the formula:



wherein R_1 is hydrogen, (C_{1-6}alkylthio, halo(C_{1-6})alkylthio, (C_{1-6})alkylsulphinyl, halo(C_{1-6})alkylsulfinyl, (C_{1-6})alkylsulphonyl, halo(C_{1-6})alkylsulphonyl or $NR_{12}R_{13}$; R_{12} and R_{13} are each independently hydrogen, (C_{1-6})alkyl, or halo(C_{1-6})alkyl; X_1 and X_2 are independently selected from the group consisting of NR_{14}, NR_{15}, O, CH_2, $CR_{18}R_{19}$, CO and C=NOR_{20}; R_2, R_3, R_4, R_5, R_6, R_7, R_8, R_9, and R_{11} are each independently selected from hydrogen, halogen, cyano, nitro, C_{1-6}alkyl, halo(C_{1-6})alkyl, (C_{1-6})alkoxy, halo(C_{1-6})alkoxy, (C_{1-6})alkoxy(C_{1-6})alkyl, halo(C_{1-6})alkoxy(C_{1-6})alkyl, (C_{1-6})alkylthio, halo(C_{1-6})alkylthio, (C_{1-6})alkylsulphinyl, halo(C_{1-6})alkylsuphinyl, (C_{1-6})alkylsulphonyl, halo(C_{1-6})alkylsulphonyl, amino, (C_{1-6})alkylamino, di(C_{1-6})alkylamino, halo(C_{1-6})alkylamino, (C_{1-6})alkylhaloalkyl(C_{1-6})amino, dihalo(C_{1-6})alkylamino, (C_{1-6})alkoxy-carbonyl, halo(C_{1-6})alkoxycarbonyl, C_{2-6}alkenyl, halo(C_{2-6})alkenyl, (C_{2-6})alkynyl, halo(C_{2-6})alkynyl; and R_{10} is halogen, halo(C_{1-6})alkyl, halo(C_{2-6})alkenyl or halo(C_{2-6})alkynyl. The substituents at 4 and 6 positions are represented by X_1-aryl and X_2-aryl, where aryl represents phenyl group having R_2, R_3, R_4, R_5, R_6, R_7, R_8, R_9, R_{10} and R_{11} substituents.

Applicants assert that Cuccia does not teach a compound of core structure $\mathbf{I}^{\mathbf{A}}$. Substituents X_1-aryl and X_2-aryl on the pyrimidine ring in Cuccia occupy the positions that correspond to R^2 and L-R^3 in $\mathbf{I}^{\mathbf{A}}$. Cuccia does not teach substituents X_1-aryl and X_2-aryl being hydrogen, halo, amino, C_{1-4}alkyl, C_{1-4}alkoxy or halo-substituted C_{1-4}alkoxy as recited for R^2 in structure $\mathbf{I}^{\mathbf{A}}$. Therefore, a compound of the structure $\mathbf{I}^{\mathbf{A}}$ is not anticipated by Cuccia.

Applicants further assert that Cuccia does not teach a compound of core structure $\mathbf{I}^{\mathbf{B}}$. Substituents X_1-aryl and X_2-aryl on the pyrimidine ring in Cuccia occupy the positions that

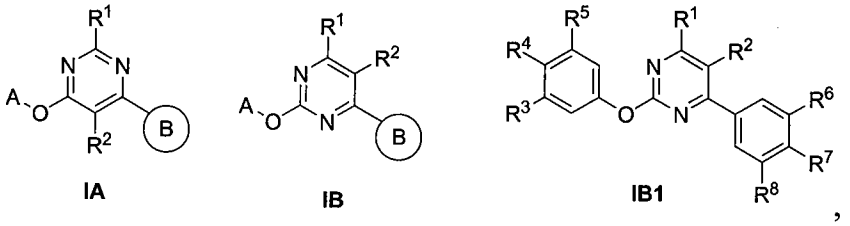
correspond to R^1 and L-R^3 in structure $\mathbf{I^B}$. Cuccia teaches X_1-aryl and X_2-aryl having substituents R_2, R_3, R_4, R_5, R_6, R_7, R_8, R_9, R_{10} and R_{11}, but does not teach that substituents R_2, R_3, R_4, R_5, R_6, R_7, R_8, R_9, R_{10} and R_{11} are hydroxy-C_{1-6}alkyl, phenyl, C_{3-8}heterocycloalkyl, $-X^3C(O)NR^8R^8$, $-X^3C(O)NR^8R^9$, $-X^3C(O)R^9$, $-X^3S(O)NR^8R^8$, $-X^3NR^8R^9$, $-X^3NR^8R^8$, $-X^3S(O)_2NR^8R^8$, $-X^3S(O)_2R^8$, $-X^3S(O)_2R^9$, $-X^3SNR^8R^8$, $-X^3ONR^8R^8$, $-X^3C(O)R^8$, $-X^3NR^8C(O)R^8$, $-X^3NR^8S(O)_2R^8$, $-X^3S(O)_2NR^8R^9$, $X^3NR^8S(O)_2R^9$, $-X^3NR^8C(O)R^9$, $-X^3NR^8C(O)NR^8R^9$, $-X^3NR^8C(O)NR^8R^8$, $=NOR^8$, $-X^3NR^8OR^8$, $-X^3NR^8(CH_2)_{1-4}NR^8R^8$, $-X^3C(O)NR^8(CH_2)_{1-4}NR^8R^8$, $-X^3C(O)NR^8(CH_2)_{1-4}R^9$, $-X^3C(O)NR^8(CH_2)_{1-4}OR^9$, $-X^3O(CH_2)_{1-4}NR^8R^8$, $-X^3C(O)NR^8(CH_2)_{1-4}OR^8$and $X^3NR^8(CH_2)_{1-4}R^9$ as recited for R^3 in amended claim 1. Therefore, a compound of structure $\mathbf{I^B}$ is not anticipated by Cuccia.

Since core structures $\mathbf{I^A}$ or $\mathbf{I^B}$ of the compounds of Formula I are not disclosed by Cuccia, claim 1 is not anticipated by Cuccia. Accordingly, Applicants respectfully request that the rejection of claim 1 under 35 U.S.C. §102(b) over Cuccia be withdrawn. Moreover, since claims 6, 9, 10 and 17 are dependent from claim 1 and, therefore, incorporate all the limitations of claim 1, claims 6, 9, 10 and 17 are not anticipated by Cuccia. Accordingly, Applicants respectfully request that the rejection of claims 1, 6, 9 10 and 17 over Cuccia under 35 U.S.C. §102(b) be withdrawn.

D. Rejection of Claims 1, 6, 9, 10 and 17 over Wood *et al.*

Claims 1, 6, 9, 10 and 17 were rejected under 35 U.S.C. §102(b) as allegedly anticipated by Wood *et al.* (U.S. Patent No. 6,306,866, hereinafter "Wood"). To the extent the rejection is applicable to the amended claims, Applicants respectfully traverse the rejection.

Applicants assert that Wood does not teach each and every element of the invention, thus Wood does not anticipate the claimed invention. Wood teaches pyrimidine derivatives having the formulae:



IA IB IB1

wherein A represents a phenyl group being substituted by one or more of the same or different substituents selected from halogen atoms, alkyl, alkoxy, cyano, nitro, haloalkyl, haloalkoxy, alkylthio, haloalkylthio, alkylsuphinyl, alkylsulphonyl and SF_5 groups. B represents a phenyl group being substituted by one or more of the same or different substituents selected from halogen atoms, alkyl, alkoxy, cyano, nitro, haloalkyl, haloalkoxy, alkylthio, haloalkylthio, alkylsulphinyl, alkylsulphonyl and SF_5 groups.

Applicants assert that the core structure $\mathbf{I^A}$ is not anticipated by a compound of formula **IA**, **IB** or **IB1** in Wood. Substituents A-O and B on the pyrimidine ring in **IA**, **IB** or **IB1** occupy the positions that correspond to R^2 and L-R^3 in structure $\mathbf{I^A}$. Formula **IA**, **IB** or **IB1** in Wood does not teach (or allow for) substituents A-O and B to be hydrogen, halo, amino, C_{1-4}alkyl, halo-substituted C_{1-4}alkyl, C_{1-4}alkoxy or halo-substituted C_{1-4}alkoxy as recited for R^2 in structure $\mathbf{I^A}$. Instead, substituents A-O and B in formula **IA** in Wood are substituted-phenoxy or substituted-phenyl groups, respectively. Thus, neither substituent A-O nor B of the formula **IA**, **IB** or **IB1** anticipates substituent R^2 in $\mathbf{I^A}$. As such, structure $\mathbf{I^A}$ is not anticipated by a compound of the formula **IA**, **IB** or **IB1** in Wood.

Applicants further asserts that the core structure $\mathbf{I^B}$ is not anticipated by a compound of formula **IA**, **IB** or **IB1** in Wood. Substituents A-O and B on the pyrimidine ring in **IA**, **IB** or **IB1** occupy the positions that correspond to R^1 and L-R^3 in structure $\mathbf{I^B}$. Wood teaches A-O and B to be substituted phenoxy or phenyl groups, wherein the substituents on the phenyl ring are halogen atoms, alkyl, alkoxy, cyano, nitro, haloalkyl, haloalkoxy, alkylthio, haloalkylthio, alkylsuphinyl, alkylsulphonyl and SF_5 groups, but **does not** teach hydroxy-C_{1-6}alkyl, phenyl, C_{3-8}heterocycloalkyl, $-X^3C(O)NR^8R^8$, $-X^3C(O)NR^8R^9$, $-X^3C(O)R^9$, $-X^3S(O)NR^8R^8$, $-X^3NR^8R^9$, $-X^3NR^8R^8$, $-X^3S(O)_2NR^8R^8$, $-X^3S(O)_2R^8$, $-X^3S(O)_2R^9$, $-X^3SNR^8R^8$, $-X^3ONR^8R^8$, $-X^3C(O)R^8$, $-X^3NR^8C(O)R^8$, $-X^3NR^8S(O)_2R^8$, $-X^3S(O)_2NR^8R^9$, $X^3NR^8S(O)_2R^9$,

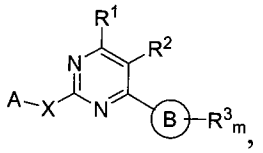
$-X^3NR^8C(O)R^9$, $-X^3NR^8C(O)NR^8R^9$, $-X^3NR^8C(O)NR^8R^8$, $=NOR^8$, $-X^3NR^8OR^8$, $-X^3NR^8(CH_2)_{1-4}NR^8R^8$, $-X^3C(O)NR^8(CH_2)_{1-4}NR^8R^8$, $-X^3C(O)NR^8(CH_2)_{1-4}R^9$, $-X^3C(O)NR^8(CH_2)_{1-4}OR^9$, $-X^3O(CH_2)_{1-4}NR^8R^8$, $-X^3C(O)NR^8(CH_2)_{1-4}OR^8$and $X^3NR^8(CH_2)_{1-4}R^9$ as recited for R^3 in structure $\mathbf{I^B}$. Therefore, compounds of the structure $\mathbf{I^B}$ are not anticipated by the compounds of formula **IA, IB** or **IB1** in Wood.

Again, since claim 1 is not anticipated by any compound of formulae **IA, IB** or **IB1** disclosed in Wood, Applicants respectfully request that the rejection of claim 1 under 35 U.S.C. §102(b) over Wood be withdrawn. Moreover, since claims 6, 9, 10 and 17 are dependent from claim 1 and, therefore, incorporate all the limitations of claim 1, claims 6, 9, 10 and 17 are not anticipated by Wood. Accordingly, Applicants respectfully request that the rejection of claims 1, 6, 9 10 and 17 over Wood under 35 U.S.C. §102(b) be withdrawn.

E. Rejection of claims 6, 9, 10 and 17 over Scheiblich *et al.*

Claims 1, 6, 9, 10 and 17 were rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Scheiblich *et al.* (U.S. Patent No. 6,313,072 hereinafter "Scheiblich"). To the extent that the rejection is applicable to the amended claims, Applicants respectfully traverse the rejection.

Applicants assert that Scheiblich does not teach each and every element of the claimed invention, thus does not anticipate the claimed invention. Scheiblich teaches a compound having the formula:



wherein A represents an optionally substituted aryl group or an optionally substituted 5- or 6-membered hetero-aromatic group or a difluorobenzodioxolyl group; B represents a pheny, pyridyl or thienyl group; R^1 represents a halogen atom or a cyano or an optionally substituted alkyl, alkenyl, alkynyl, alkoxyalkyl, haloalkyl, alkoxy, haloalkoxy, alkylthio, alkylamino or dialkylamino group; X represents an oxygen or sulfur atom; and R^3 independently represents a halogen atom, an optionally substituted alkyl, alkenyl, alkynyl,

alkoxy, alkoxyalkyl, alkoxyakoxy, alkylthio, alkylsulfinyl, alkylsulphonyl group or a nitro, cyano, haloalkyl, haloalkoxy, haloalkylthio or SF_5 group.

Applicants assert that Scheiblich does not teach a compound having the structure $\mathbf{I^A}$. Substituents R^1 and $\text{(B)}-R^3{}_m$ in Scheiblich correspond to R^2 and L-R^3 in structure $\mathbf{I^A}$. Scheiblich teaches B to be phenyl, pyridyl or thienyl group having substituents $R^3{}_m$, but does not teach (or allow for) substituents $R^3{}_m$ in $\text{(B)}-R^3{}_m$ to be hydroxy-$C_{1\text{-}6}$alkyl, phenyl, $C_{3\text{-}8}$heterocycloalkyl, $-X^3C(O)NR^8R^8$, $-X^3C(O)NR^8R^9$, $-X^3C(O)R^9$, $-X^3S(O)NR^8R^8$, $-X^3NR^8R^9$, $-X^3NR^8R^8$, $-X^3S(O)_2NR^8R^8$, $-X^3S(O)_2R^8$, $-X^3S(O)_2R^9$, $-X^3SNR^8R^8$, $-X^3ONR^8R^8$, $-X^3C(O)R^8$, $-X^3NR^8C(O)R^8$, $-X^3NR^8S(O)_2R^8$, $-X^3S(O)_2NR^8R^9$, $X^3NR^8S(O)_2R^9$, $-X^3NR^8C(O)R^9$, $-X^3NR^8C(O)NR^8R^9$, $-X^3NR^8C(O)NR^8R^8$, $=NOR^8$, $-X^3NR^8OR^8$, $-X^3NR^8(CH_2)_{1\text{-}4}NR^8R^8$, $-X^3C(O)NR^8(CH_2)_{1\text{-}4}NR^8R^8$, $-X^3C(O)NR^8(CH_2)_{1\text{-}4}R^9$, $-X^3C(O)NR^8(CH_2)_{1\text{-}4}OR^9$, $-X^3O(CH_2)_{1\text{-}4}NR^8R^8$, $-X^3C(O)NR^8(CH_2)_{1\text{-}4}OR^8$and $X^3NR^8(CH_2)_{1\text{-}4}R^9$ as recited for R^3 in amended claim 1. Therefore, a compound of structure $\mathbf{I^A}$ is not anticipated by Scheiblich.

Applicants assert that Scheiblich does not teach a compound having the structure $\mathbf{I^B}$. Substituent A-X in Scheiblich corresponds to R^2 in structure $\mathbf{I^B}$. Scheiblich does not teach (or allow for) A-X to be hydrogen, halo, amino, $C_{1\text{-}4}$alkyl, halo-substituted $C_{1\text{-}4}$alkyl, $C_{1\text{-}4}$alkoxy and halo-substituted $C_{1\text{-}4}$alkoxy as recited for R^2 in structure $\mathbf{I^B}$. Therefore, structure $\mathbf{I^B}$ is not anticipated by Scheiblich.

Since core structures $\mathbf{I^A}$ or $\mathbf{I^B}$ of the compounds of Formula I are not disclosed by Scheiblich, claim 1 is not anticipated by Scheiblich. Accordingly, Applicants respectfully request that the rejection of claim 1 under 35 U.S.C. §102(b) over Scheiblich be withdrawn. Moreover, since claims 6, 9, 10 and 17 are dependent from claim 1 and, therefore, incorporate all the limitations of claim 1, claims 6, 9, 10 and 17 are not anticipated by Scheiblich. Accordingly, Applicants respectfully request that the rejection of claims 1, 6, 9 10 and 17 over Scheiblich under 35 U.S.C. §102(b) be withdrawn.

III. Claim Rejections under 35 U.S.C. § 103(a)

A. Claim Rejection over Boykin

Claims 1, 6-8 and 11 were rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Boykin. To the extent the rejection is applicable to the amended set of claims, Applicants respectfully traverse the rejection.

> As set forth in MPEP §2142: To establish a prima facie case of obviousness, three criteria must be met. There must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference must teach or suggest all the claim limitations.

As explained above, Boykin does not teach all the claim limitations of claims 1, 6-8 and 11. Moreover, in view of the structural differences between the presently claimed compounds and the Boykin compounds, Applicants respectfully submit that the claimed compounds are non-obvious and, thus, patentable. As such, Applicants respectfully request that the rejection of claims 1, 6-8 and 11 under 35 U.S.C. §103(a) over Boykin be withdrawn.

B. Claim rejection over Carling

Claims 1, 6-8 and 11 were rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Carling. To the extent the rejection is applicable to the amended set of claims, Applicants respectfully traverse the rejection.

As explained above, Carling does not teach all the claim limitations of claims 1, 6-8 and 11. Moreover, in view of the structural differences between the presently claimed compounds and the Carling compounds, Applicants respectfully submit that the claimed compounds are non-obvious and, thus, patentable. As such, Applicants respectfully request that the rejection of claims 1, 6-8 and 11 under 35 U.S.C. §103(a) over Carling be withdrawn.

C. Claim rejection over Cuccia

Claims 1, 6, 9, 10 and 17 were rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Cuccia. To the extent the rejection is applicable to the amended set of claims, Applicants respectfully traverse the rejection.

As explained above, Cuccia does not teach all the claim limitations of claims 1, 6, 9, 10 and 17. Moreover, in view of the structural differences between the presently claimed compounds and the Cuccia compounds, Applicants respectfully submit that the claimed compounds are non-obvious and, thus, patentable. As such, Applicants respectfully request that the rejection of claims 1, 6-8 and 11 under 35 U.S.C. §103(a) over Cuccia be withdrawn.

D. Claim rejection over Wood

Claims 1, 6, 9, 10 and 17 were rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Wood. To the extent the rejection is applicable to the amended set of claims, Applicants respectfully traverse the rejection.

As explained above, Wood does not teach all the claim limitations of claims 1, 6, 9, 10 and 17. Moreover, in view of the structural differences between the presently claimed compounds and the Wood compounds, Applicants respectfully submit that the claimed compounds are non-obvious and, thus, patentable. As such, Applicants respectfully request that the rejection of claims 1, 6-8 and 11 under 35 U.S.C. §103(a) over Wood be withdrawn.

E. Claim rejection over Scheiblich

Claims 1, 6-8 and 11 were rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Scheiblich. To the extent the rejection is applicable to the amended set of claims, Applicants respectfully traverse the rejection.

As explained above, Scheiblich does not teach all the claim limitations of claims 1, 6-8, and 11. Moreover, in view of the structural differences between the presently claimed compounds and the Scheiblich compounds, Applicants respectfully submit that the claimed compounds are non-obvious and, thus, patentable. As such, Applicants respectfully request that the rejection of claims 1, 6-8 and 11 under 35 U.S.C. §103(a) over Scheiblich be withdrawn.

IV. Double Patenting

Claims 1 and 6-17 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 57-72 of co-pending Application No. 10/270,030.

Because this is a provisional rejection, Applicants respectfully request that the Examiner hold this rejection in abeyance until there is an indication of allowable subject matter. At that time, Applicants will cancel the conflicting claims or file a Terminal Disclaimer.

V. Claim Objection

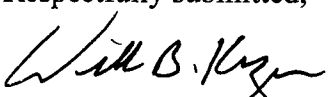
Claim 11 was objected to as allegedly for lacking an inert or acceptable carrier. In response, Applicants have amended claim 11 to incorporate the Examiner's suggestion. In view of the amendment, Applicants respectfully request that the claim objection be withdrawn.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-472-5000.

Respectfully submitted,



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